

## RIGHT VENTRICULAR HYPERTROPHY AND THE SMALL PULMONARY ARTERIES IN CHRONIC LUNG DISEASE

BY

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Changes in the small muscular arteries of the lungs can be found in many forms of chronic lung disease. In primary pulmonary hypertension a characteristic form of medial hypertrophy occurs (Harris and Heath, 1962). In the massive form of coalworkers' pneumoconiosis there occurs a progressive stenosing arterial lesion which is not seen in the simple form of the disease (Thomas and James, 1958). Arteritis accompanies other forms of fibrosis and is particularly severe in areas of bronchiectasis. Changes occur in the small vessels in chronic bronchitis and emphysema, and the lesions vary in severity from case to case and in different areas of the same lung. Harris and Heath (1962) remark that in the great majority of cases of emphysema the small blood vessels of the lung show little or no change that might be due to pulmonary hypertension.

During injection studies of the small pulmonary arteries we found a considerable reduction of the peripheral arterial bed in emphysema (James, Owen, and Thomas, 1960). Microscopy of the affected areas showed that many of the small arteries were thickened and narrowed. In contrast a lung from a case of asthma of 30 years' duration had a normal arterial bed. These findings prompted us to study the clinical and histological data in 91 cases of chronic lung disease that have come to autopsy. The series included 54 in which chronic bronchitis and right ventricular hypertrophy were present with or without emphysema. There were also 12 cases of asthma, 18 of bronchiectasis, and 7 examples of less common conditions.

We diagnosed chronic bronchitis when three conditions were satisfied: (1) no other chronic lung disease, except emphysema; (2) cough with sputum occurring on most days for at least three months in the year during at least two years; and (3) gross macroscopic and microscopic changes satisfied one of us (W.R.L.J.) that a diagnosis of chronic bronchitis was tenable.

The observations leading to a pathological diagnosis of chronic bronchitis macroscopically were thick-walled bronchi with small lumina, bronchial diverticula, a thick soft congested mucosa and mucopus or excessive mucus in the lumina. The histological criteria were enlargement of the mucous glands (Reid, 1960), engorgement of the intramural vessels, abnormalities of the mucous membrane, and chronic inflammatory cells in the submucosa. Histological diagnosis involves some subjective assessments and it can be uncertain. We have found the clinical criteria and post-mortem exclusion of other diseases to be more reliable diagnostic aids.

Emphysema is a pathological diagnosis. It is characterized by an increase beyond the normal in the size of air-spaces distal to the terminal bronchioles either from dilatation or from destruction of their walls (Ciba Symposium, 1958).

### METHOD

At autopsy the emphysema was graded macroscopically and subjectively as absent, slight, moderate, or severe. The grade "slight" refers to lungs in which less than one-fifth of the cut surface of the whole lung

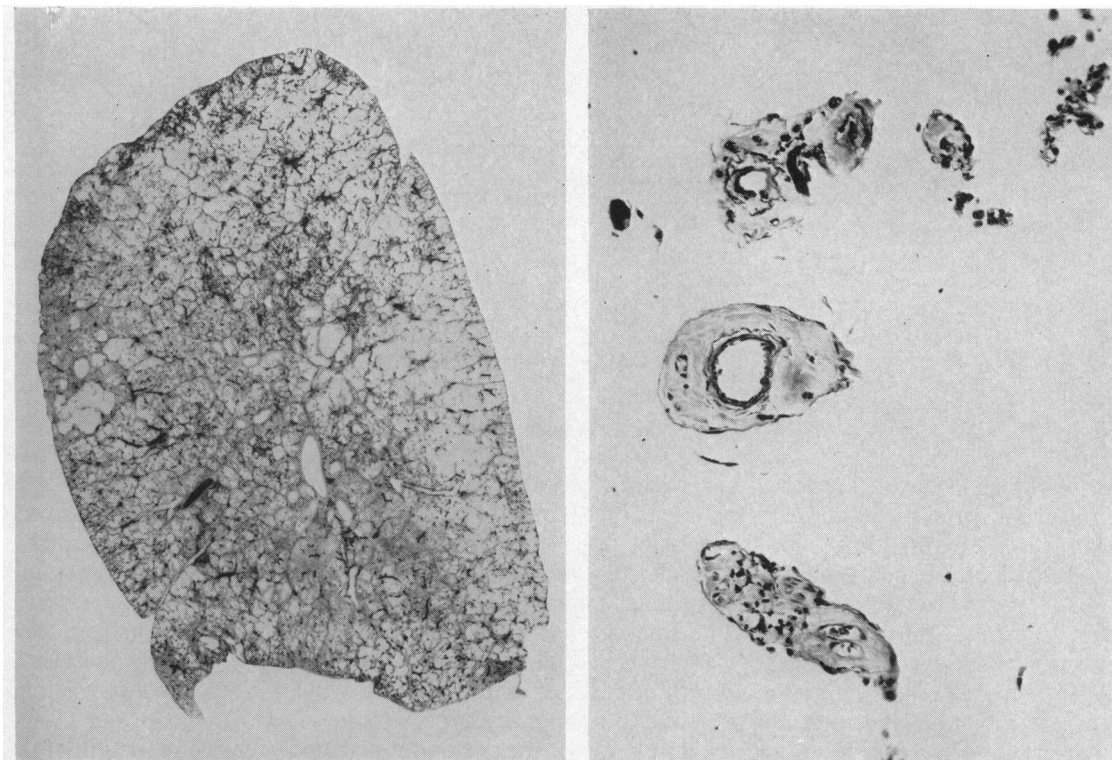


FIG. 1(A).—Section of a lung from a man aged 48 who had had signs of bronchitis and emphysema for 8 years. The P.A. pressure was raised at rest and the right ventricle was 6 mm. thick.

(B).—Stenosed small arteries from the lung shown in (A). The lumen of the largest vessel is approximately  $50\ \mu$ . (Hæmalum and eosin;  $\times 115$ .)

was emphysematous. This has been described as subclinical emphysema (Snider, Brody, and Doctor, 1962).

Right ventricular hypertrophy was assessed by measuring the wall thickness 3 cm. below the pulmonary valve in line with the course of the pulmonary conus.

Histological sections were stained with hæmalum-eosin and Verhoeff-van Gieson. Thickening of the walls of the 100 to 300  $\mu$  arteries was graded as absent, slight, moderate, and severe. Slight intimal thickening is such a common finding in aged lungs that for the purpose of this study those with slight changes were grouped as normal.

## RESULTS

*Bronchitis with Emphysema.* There were 32 examples of chronic bronchitis with moderate or severe emphysema. The range of right ventricular thickness was 5 to 10 mm. In 22 of the 32 cases we observed moderate or severe small artery thickening but in the other 10 the vessels were normal. The latter association of normal vessels and right ventricular hypertrophy was of special interest. These patients had had long histories of moderate bronchitis permitting normal activity interrupted by short periods of severe disability with hypoxia. In those with serial electrocardiograms there was conversion to pulmonary heart disease pattern in the two years before death.

The 22 cases with bronchitis, emphysema, and vascular thickening had all suffered increasing dyspnoea for many years (Fig. 1). For example, a painter of 48 had had cough and wheezing for eight years and severe dyspnoea for four years, and showed severely impaired pulmonary function: vital capacity 1.25 litres, maximum breathing capacity 17 litres, forced expiratory volume at one

second 0.5 litres,  $P_{CO_2}$  42 mm., oxygen saturation 79 per cent, and mean pulmonary arterial pressure 36 mm. Hg.

*Chronic Bronchitis Without Emphysema.* There were 22 cases of chronic bronchitis in which emphysema was absent or slight. The range of right ventricular thickness was 5 to 9 mm.

In nine the small arteries and arterioles were normal or virtually so. In the other 13 there was vascular thickening of moderate or severe degree (Fig. 2 and 3).

*Asthma.* The series included 12 patients with asthma. In all of them attacks had occurred for more than four years. In 7 the duration was more than twenty years. In none did the electrocardiogram suggest right heart strain. None had right ventricular hypertrophy and in all the pulmonary arteries were normal (Fig. 4).

*Bronchiectasis.* All 18 patients had right ventricular hypertrophy. In the affected segments of lung inflammatory arteritis with various degrees of resolution was observed. The unaffected parts of the lung showed normal small arteries.

*Other Lung Diseases.* The remaining seven cases had all been diagnosed as chronic bronchitis at some stage of their illnesses.

Two were instances of kyphoscoliotic heart disease with right ventricular hypertrophy. The lungs were small but the microscopic structure of the air spaces, bronchi, and vessels was normal.

Two had right ventricular hypertrophy and severe concentric hypertrophy of the pulmonary arteries. No other cardiac or pulmonary lesion was found, and these were regarded as examples of primary pulmonary hypertension.

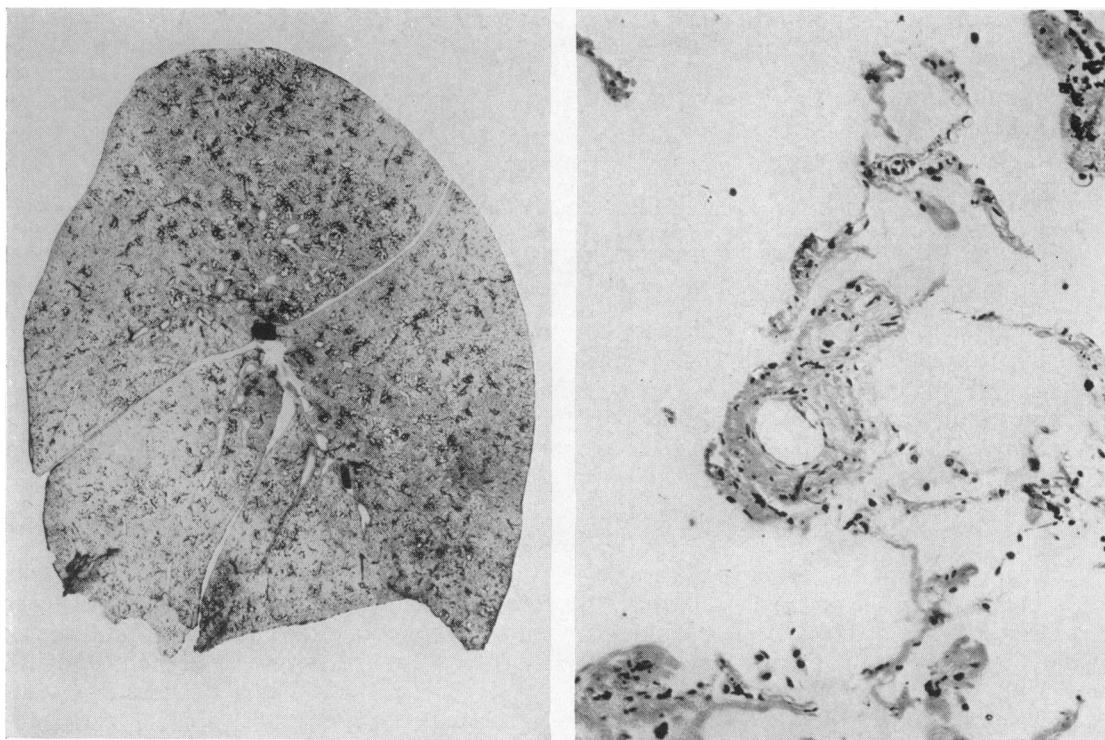


FIG. 2(A).—Section of a lung from a man aged 69 who died in congestive cardiac failure after a 22-year history of chronic bronchitis. There was slight emphysema. The right ventricle was heavier than the left.

(B).—A thickened arteriole from the lung illustrated in (A). The lumen diameter is  $60\mu$ . (Hæmalum and eosin;  $\times 170$ .)

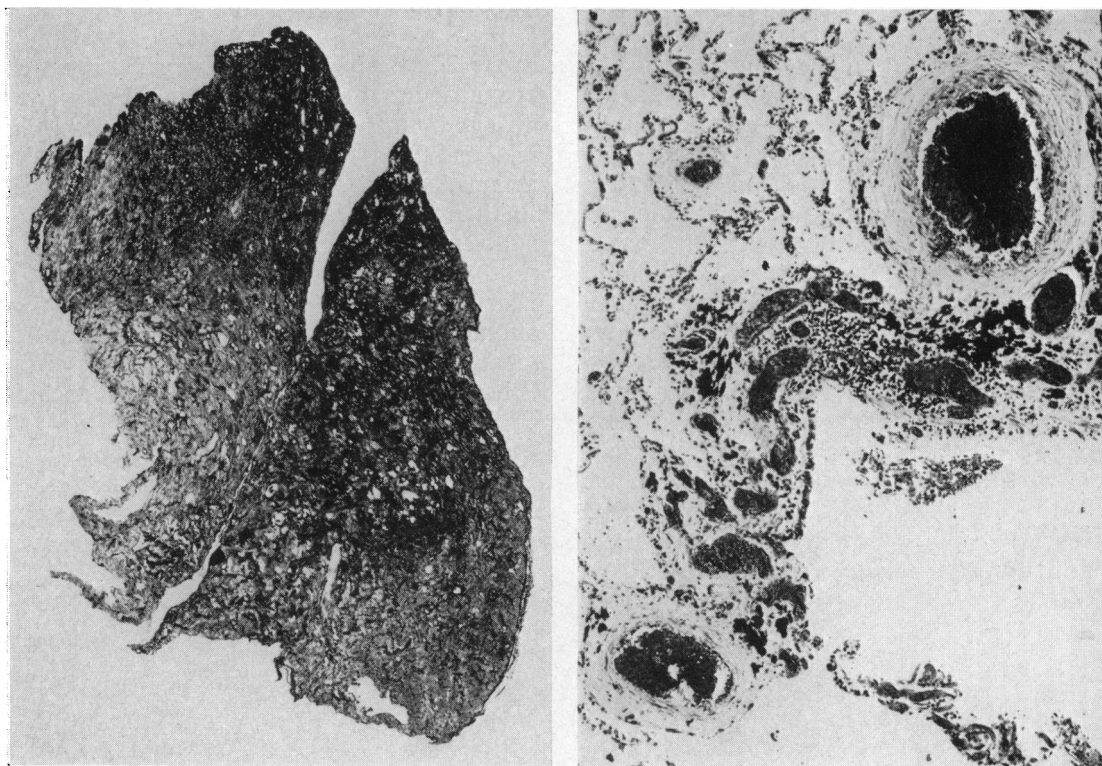


FIG. 3(A).—Section of a lung from a man aged 56 who had been treated for chronic bronchitis for over 20 years. Physiology and histology confirmed the diagnosis. The lung was free from emphysema. The right ventricle measured 7 mm.

(B).—Thickened small arteries near a chronically inflamed bronchiole from the lung shown in (A). The maximum lumen diameter of the largest vessel is  $260\ \mu$ . (H&E;  $\times 80$ .)

Two were cases of widespread pulmonary fibrosis with right heart enlargement in which the cause of the fibrosis could not be determined. The histology was not that of the Hamman-Rich syndrome. The severe pulmonary vascular lesions suggested that the cause of the fibrosis in both was unresolved pneumonia, but there was no clinical history of this.

One was a case of "farmer's lung." Pulmonary fibrosis, severe vascular thickening, and right ventricular hypertrophy were present.

#### DISCUSSION

Clinical and physiological study of chronic obstructive airway disease has shown some patients with a rise in the mean pulmonary arterial pressure when the arterial oxygen saturation was over 90 per cent. When exercised while breathing oxygen they showed a further increase of pulmonary arterial pressure to twice the resting value without a fall of arterial oxygen saturation (Thomas, Cotes, and Pisa, 1962). This argues the presence of a mechanism other than hypoxic vasoconstriction. There seems to be a lesion that renders the vascular bed inelastic and unable to permit increased flow on exercise without a considerable increase in pulmonary arterial pressure. There is no doubt also that when hypoxia occurs, further rises in pressure result.

Some cases of chronic bronchitis showed pulmonary arteriolar stenosis: others did not. Those with stenosis had some degree of pulmonary arterial hypertension at rest and more severe hypertension on exercise. Pulmonary hypertension may be due to anatomical obstructive arterial

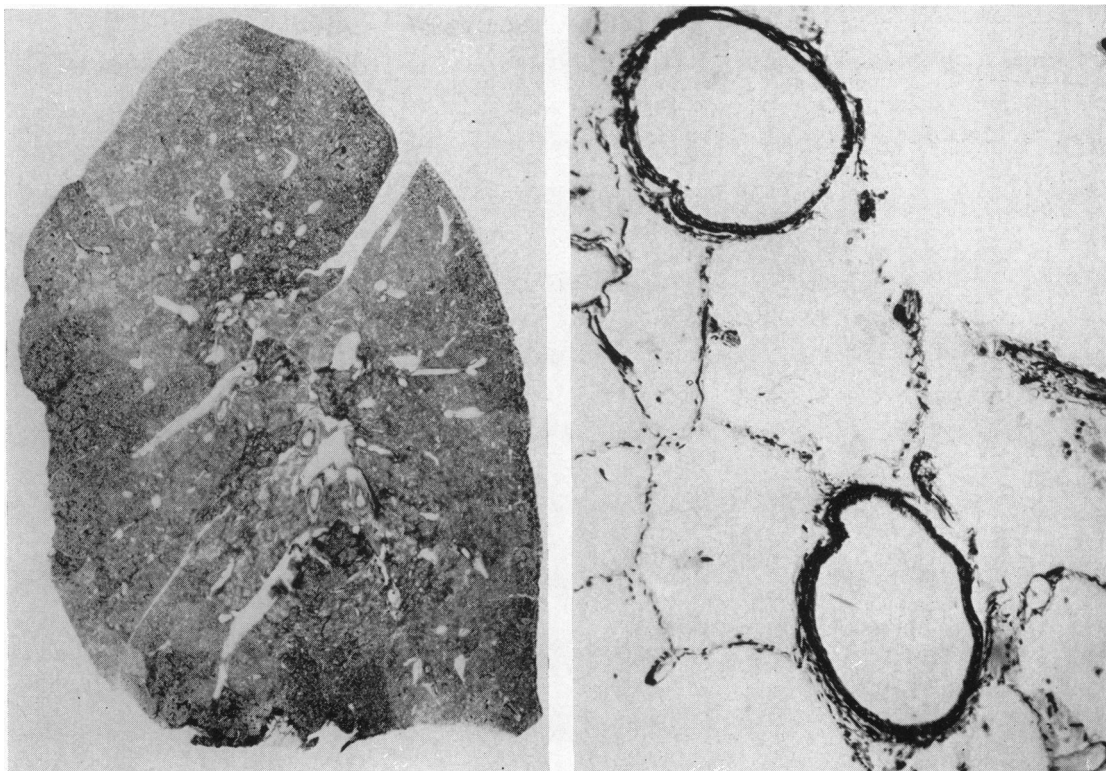


FIG. 4(A).—Section of a lung from a woman aged 57 who had had asthma for over 30 years. The lung was free from emphysema and the right ventricle was normal. (B).—Normal small arteries from the specimen shown in (A). The vessels are approximately  $220\ \mu$  in diameter. (Verhoeff—van Gieson;  $\times 122$ .)

disease or hypoxic vasoconstriction. This study suggests that in many cases of bronchitis and emphysema both causes are present. In emphysema part of the capillary bed degenerates. In chronic bronchitis and in emphysema arteriolar degeneration is sometimes so severe that the arterioles are barely recognizable.

It is unlikely that the arteriolar lesion is due to preceding pulmonary hypertension. The lesion differs from that seen in the pulmonary vessels in congenital heart disease with pulmonary hypertension, and also from the renal arteriolosclerosis of benign systemic hypertension. It seems to us more likely that some cases of chronic bronchitis are complicated by arteriolar thickening of infective origin, and that this is rare in arteries over  $300\ \mu$  in diameter but common in smaller arteries and arterioles.

#### SUMMARY

Ninety-one patients with chronic lung disease were studied clinically and after autopsy. The results show that in some cases of emphysema and in some cases of chronic bronchitis there is organic stenosis of the small pulmonary arteries and arterioles. The authors suggest that these anatomical lesions cause significant obstruction and contribute to pulmonary hypertension.

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